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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,314	12/08/2006	Peter Leonard Bergquist	ALAR4.001APC	3637

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/530,314	BERGQUIST ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-46* is/are pending in the application.

4a) Of the above claim(s) *45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/30/2006 & 3/6/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 28, 44 in the reply filed on November 29, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Accordingly, claims 45 and 46 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-27 have been canceled.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy is noted in the instant application.

Claim Rejections - 35 USC § 102(b)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 29-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (citation made of record in IDS filed 03/06.2006).

With regards to claim 28, Zhang et al teach a method for producing mutant genes encoding an enzyme, the method comprising: (a) introducing one or more mutations into a gene encoding an enzyme to form a plurality of mutated genes; (b) providing the mutated genes to host microorganisms by inserting the mutated genes into vectors and

transforming the microorganisms with the vectors; (c) culturing the host microorganisms containing the vectors in the presence of a substrate for the enzyme under conditions suitable for activity of the enzyme such that a microorganism expressing a functional enzyme from a mutated gene has a detectable characteristic; and (d) obtaining host microorganisms expressing a functional enzyme without selecting microorganisms on the basis of an altered or defined level of enzyme activity compared with a corresponding wild type enzyme (see entire reference, especially page 4505, "Materials and Method).

With regards to claim 29, Zhang et al. teach the method according to claim 28 further comprising: (e) recovering the vectors from the host microorganisms expressing a functional enzyme (see "Materials and Methods", page 4505).

With regards to claim 30, Zhang et al. teach the method according to claim 28 further comprising: (f) obtaining a combined pool of mutated genes encoding functional enzymes from the microorganisms in step (d) and repeating steps (a) to (d) to form a library of microorganisms containing a plurality of mutant genes expressing a functional enzyme (see page 4506 col. 1).

With regards to claim 31, Zhang et al. teach the method according to claim 30 further comprising: (g) screening the library of microorganisms to obtain a mutant gene encoding a functional enzyme (abstract and "Materials and Methods: see also Figure 1).

With regards to claim 32, Zhang et al. teach the method according to claim 28 wherein step (a) is carried out by gene shuffling (page 4504, col. 2 and Figure 1).

With regards to claim 33, Zhang et al teach the method according to claim 28 wherein the vector is a plasmid or virus and the host microorganism is a bacterium (abstract and page 4505, col. 1, first paragraph under "Materials and Methods").

With regards to claim 34 Zhang et al. teaches the method according to claim 33 wherein the bacterium is Escherichia coli (Abstract and page 4505, col. 1, first paragraph under "Materials and Methods").

With regards to claim 35, Zhang et al. teaches the method according to claim 33 wherein host microorganisms are cultured in a liquid medium ("Materials and Methods")..

With regards to claim 36, Zhang et al. teach the method according to claim 28 wherein the detectable characteristic of the microorganism is derived from enzymatic action on the substrate ("Materials and Methods").

With regards to claim 37, Zhang et al teach the method according to claim 36, wherein the enzyme can form a chromogenic phenotype or character in the host microorganism (Materials and Methods, col. 2).

With regards to claim 38, Zhang et al. teach the method according to claim 37 wherein the host microorganism is selected by changes in its spectral characteristics due to action of the enzyme on the substrate (page 4505, "Materials and Methods" and page 4506, col. 1).

With regards to claim 39, Zhang et al teach the method according to claim 38, wherein the enzyme is capable of acting on an X-sugar (Materials and Methods, page 4505).

With regards to claim 40, Zhang et al teach the method according to claim 39 wherein the substrate is an indoxyl- linked compound ("Materials and Methods").

With regards to claim 41, Zhang et al teach the method according to claim 40 wherein the enzyme acting on an indoxyl-linked substrate is form of beta-galactosidases (Materials and Methods at page 4505 and section entitled "Kinetics" at page 4506-4507).

With regards to claim 42, Zhang et al teach the method according to claim 41 wherein the enzyme is capable of acting on 5-Bromo-4-chloro-3-indolyl-D-galactopyranoside which forms a chromogen upon enzymatic hydrolysis (page 4505, col. 1 of "Materials and Methods")..

With regards to claim 43, Zhang et al teach the method according to claim 28 wherein the enzyme substrate is retained on, or within the cell, in liquid culture (page 4506, col. 1). Therefore, Zhang et al meet the limitations of the claims as currently written.

5. Claims 28-31, 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Rai et al., (citation made of record on IDS filed 3/6/2006). With regards to claim 28, Rai et al. teach a method for producing mutant genes encoding an enzyme, the method comprising: (a) introducing one or more mutations into a gene encoding an enzyme to form a plurality of mutated genes; (b) providing the mutated genes to host microorganisms by inserting the mutated genes into vectors and transforming the

microorganisms with the vectors; (c) culturing the host microorganisms containing the vectors in the presence of a substrate for the enzyme under conditions suitable for activity of the enzyme such that a microorganism expressing a functional enzyme from a mutated gene has a detectable characteristic; and (d) obtaining host microorganisms expressing a functional enzyme without selecting microorganisms on the basis of an altered or defined level of enzyme activity compared with a corresponding wild type enzyme (pages 5-11 at the steps (a) through (d)).

With regards to claim 29, Rai et al. teach the method according to claim 28 further comprising: (e) recovering the vectors from the host microorganisms expressing a functional enzyme (page 11, second paragraph).

With regards to claim 30, Rai et al. teach the method according to claim 28 further comprising: (f) obtaining a combined pool of mutated genes encoding functional enzymes from the microorganisms in step (d) and repeating steps (a) to (d) to form a library of microorganisms containing a plurality of mutant genes expressing a functional enzyme (page 13-14).

With regards to claim 31, Rai et al. teach the method according to claim 30 further comprising: (g) screening the library of microorganisms to obtain a mutant gene encoding a functional enzyme (pages 11-14).

With regards to claim 33, Rai et al. teach the method according to claim 28 wherein the vector is a plasmid or virus and the host microorganism is a bacterium (page 7 and 8).

With regards to claim 34, Rai et al. teach the method according to claim 33 wherein the bacterium is *Escherichia coli* (pages 7 and 8).

With regards to claim 36, Rai et al. teach the method according to claim 28 wherein the detectable characteristic of the microorganism is derived from enzymatic action on the substrate (pages 5-11). Therefore, Rai et al. meets the limitations of the claims as currently written.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al in view of Rice et al (PNAS, vol. 89, pages 5467-5471, June 1992). With regards to claim 28, Zhang et al teach a method for producing mutant genes encoding an enzyme as previously discussed above. Zhang et al do not expressly teach wherein the host are obtained by sorting by flow cytometry.

Rice et al teach a general method for screening randomly mutagenized expression libraries in host cells by flow cytometry (FACS) (see abstract and Materials and Methods; see also Figure 1 at page 5468). Rice et al teach that PCR/FACS random mutagenesis methodology permits rapid sorting of target proteins directly by expression in the host cells (page 5471). Thus, it would have been obvious to one or ordinary skill in the art at the time of the claimed invention to apply the flow cytometry techniques of Rice to the mutagenesis method of Zhang for the predictably results of enabling rapid sorting of the host microorganisms as suggested by Rice.

Conclusion

9. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Patent Examiner
Art Unit 1637